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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,233	09/25/2006	Stephen Robert Wedge	056291-5303	3400

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MORGAN LEWIS & BOCKIUS LLP
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WASHINGTON, DC 20004

EXAMINER

FRAZIER, BARBARA S

ART UNIT	PAPER NUMBER
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1611

MAIL DATE	DELIVERY MODE
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10/28/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,233	Applicant(s) WEDGE, STEPHEN ROBERT	
	Examiner BARBARA FRAZIER	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-17, 21 and 24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-17, 21 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/29/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Claims

1. Claims 15-17, 21, and 24 are pending in this application.
2. Cancellation of claims 18 and 20 is acknowledged. Claims 1-14, 19, 22, and 23 stand canceled.
3. Claims 15-17, 21, and 24 are examined.

Priority

4. Applicant's comments regarding priority are duly noted; the earliest effective US filing date afforded the instantly claimed invention is 3/22/2005, the filing date of PCT/GB05/01080.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

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be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. The provisional rejection of claims 15-21 and 24 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending application No. 10/563,439; 10/563,440; 10/594,233; 10/594,234; 11/663,912 in view of Lee (US 2002/0002162) is withdrawn in favor of the new grounds of rejection below:

7. Claims 15-17, 21, and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 4, and 15 of copending Application No. 10/563,439, or alternatively over claims 12-18 of 10/594,234; claims 21-24, 27, 28, and 31-34 of 10/594,235; claims 11, 12, and 15-24 of 11/994,824; claims 11-17 of 12/158,266; or claims 13-21 of 12/408,833 in view of Hennequin et al (WO 00/47212).

The claimed invention is drawn to method for the treatment of a solid tumor cancer in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of AZD2171, or a pharmaceutically acceptable salt thereof, before, after, or simultaneously with an effective amount of one of 5-FU, CPT-11, or 5-FU and CPT-11 (see claim 1).

Copending application 10/563,439 (or alternatively the claims of 10/594,234; 10/594,235; 11/994,824; 12/158,266; or 12/408,833) claims a method for the treatment of a cancer in a warm-blooded animal in need thereof which comprises administering to

said mammal an effective amount of AZD2171 with another therapeutic agent, optionally with an effective amount of ionizing radiation.

The copending applications do not claim the administration of CPT-11 and/or 5-FU with the AZD2171.

Hennequin et al teach administration of quinazoline derivatives as angiogenesis inhibitors, such as solid tumors (abstract and page 83), and exemplify AZD2171 (Example 240). Hennequin et al further teach that, in the field of medical oncology, it is normal practice to use a combination of different forms of treatment to treat each patient with cancer, including radiotherapy and chemotherapy; antiproliferative/antineoplastic drugs and combinations thereof which may be used include 5-fluorouracil (5-FU) and irinotecan (CPT-11) (see pages 85 and 86).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to administer 5-fluorouracil and/or irinotecan with AZD2171 of the copending applications; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because Hennequin et al fairly teach and suggest the use of said compounds in conjoint treatment with quinazoline derivatives such as AZD2171.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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9. Applicant's arguments, particularly with respect to the Hilberg reference (pages 5 and 6 of Remarks filed 4/29/09), with respect to the rejection of claims 15-18, 20-21, and 24 under 35 USC 103(a) have been fully considered and are persuasive.

Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Hennequin et al (WO 00/47212).

10. Claims 15-17, 21, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hennequin et al (WO 00/47212).

The claimed invention is drawn to method for the treatment of a solid tumor cancer in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of AZD2171, or a pharmaceutically acceptable salt thereof, before, after, or simultaneously with an effective amount of one of 5-FU, CPT-11, or 5-FU and CPT-11 (see claim 1).

Hennequin et al teach administration of quinazoline derivatives as angiogenesis inhibitors, such as solid tumors (abstract and pages 83 and 86), and exemplify AZD2171 (Example 240). Hennequin et al further teach that, in the field of medical oncology, it is normal practice to use a combination of different forms of treatment to treat each patient with cancer, including radiotherapy and chemotherapy; antiproliferative/antineoplastic drugs and combinations thereof which may be used include 5-fluorouracil (5-FU) and irinotecan (CPT-11) (see pages 85 and 86).

Hennequin et al do not specifically teach the combination of AZD2171 with 5-fluorouracil and/or irinotecan.

However, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to administer 5-fluorouracil and/or irinotecan with AZD2171; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because Hennequin et al fairly teach and suggest the administration of antiproliferative/antineoplastic drugs and combinations thereof including 5-fluorouracil (5-FU) and irinotecan (CPT-11), such that it would be within the purview of the skilled artisan to select said compounds for administration by routine experimentation, in order to optimize the efficacy of the resultant composition.

Regarding claim 16, Hennequin et al teach that radiotherapy may be used in conjoint treatment with the selected chemotherapy (page 85).

Regarding claim 17, Hennequin et al teach the compound AZD2171 formed as its free base (Example 240).

Regarding claims 21 and 24, Hennequin et al teach that the compounds may be used to treat solid tumors of, for example, the colon, breast, prostate, lungs and skin (page 86).

Response to Data in the Specification

11. Applicant states in the specification that “significantly better” results are achieved with the combination of AZD2171 with 5-FU and/or CPT-11 than the use of any one agent alone (see page 4, lines 15-28, pages 34-39, and Figures 1-4).

Applicant’s data in the specification has been fully considered, but is not deemed persuasive for overcoming the rejection.

It should first be noted that Hennequin et al teach that, in the field of medical oncology, it is normal practice to use a combination of different forms of treatment to treat each patient with cancer, including radiotherapy and chemotherapy (page 85). Therefore, one skilled in the art would reasonably expect an improved result when using a combination of treatments versus a single treatment alone.

It is further noted that, of the dosages administered in the data for AZD2171 (1.5 mg/kg and 3 mg/kg), only one dosage is considered to be "therapeutically effective", since the specification elsewhere teaches that therapeutically effective dosages of AZD2171 are in the range of 0.01-1.5 mg/kg (see page 31, lines 20-25 of the specification).

Regarding the data for the administration of 1.5 mg/kg AZD2171 with 50 mg/kg 5-FU(Figure 2), these results do not appear to show "significantly better" results over the use of AZD2171 alone; the results up to day 25 appear to overlap statistically, and at day 25, there appears to be no improved effect from the combination of AZD2171 and 5-FU over the use of AZD2171 alone.

Regarding the data for the administration of 1.5 mg/kg AZD2171 with 25 mg/kg CPT-11 (Figure 4), the results are not commensurate in scope with the claims as currently written. First, only 1.5 mg/kg of AZD2171 is tested, but the specification teaches that an "effective dose" (as currently claimed) is 0.01-1.5 mg/kg (page 31); therefore, the full range of effective amount has not been tested, and it is not clear that one skilled in the art could ascertain a trend from the single dosage tested to extend the probative value thereof. Second, only one dosage of CPT-11 is tested (25 mg/kg), but

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the specification teaches that CPT-11 may be administered “in accordance with any known route of administration and dosage”, for example 350 mg/m² as an intravenous infusion (page 31); therefore, it is not clear if the full range of effective amounts have been tested, and it is not clear that one skilled in the art could ascertain a trend from the single dosage tested to extend the probative value thereof. Third, only one type of cancer is tested (colon tumor xenografts); since different protocols are used to treat different cancers, it is not clear that one skilled in the art could ascertain a trend from the single type of cancer tested to extend the probative value thereof to other types of cancers.

Additionally, Applicant has not tested the combination of AZD2171 with 5-FU and CPT-11, or any of the combinations with ionizing radiation, and therefore it cannot be determined if any of said combinations produce “significantly better” results, as Applicant asserts.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Ashwin Mehta/
Primary Examiner, Technology Center 1600